

REMARKS

The Office Action of February 5, 2003 presents the examination of claims 1-6. Claims 1, 5, and 6 are amended to improve the grammar thereof and place the claims into a better position for Appeal. Claims 9-11 are added. Support for claims 9-11 is found in claims 1, 5, and 6, respectively. No new matter is inserted into the application.

Interview

Applicants' representative thanks the Examiner for the interview held on May 29, 2003.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner maintains the rejection of claims 1-6 for allegedly containing new matter not described in the specification. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Specifically, the Examiner maintains his assertion that the negative limitation "excluding the addition of any degradation-inhibiting agents" is not found in the specification. Applicants strongly disagree.

The phrase "excluding the addition" of any degradation-inhibiting agents is amended to "in the absence" of any degradation-inhibiting agents. Support for the absence of any degradation-inhibiting agents is found in the specification as follows.

- On page 2, lines 3-6, the specification discloses that, in order to correctly measure the concentration of natriuretic peptides, prior methods required the addition of degradation-inhibiting agents, such as aprotinin. The specification states that these methods are disadvantageous because they were complicated and required too many steps to perform.
- Page 3, lines 2-9, the specification discloses that the present invention eliminates the complicated handling of specimens described above by using the containers described.
- Page 4, lines 18-19, the specification states, "This invention relates to a measurement of natriuretic peptide in specimens which do not contain aprotinin." Thus, the specification literally states that the specimen does not contain this degradation-inhibiting agent.

- Examples 1-3, pages 6-8, the specification discloses experiments for the measurement of brain natriuretic peptide (BNP). In Example 1, BNP is measured in glass tubes, in Example 2, BNP is measured in polyethylene terephthalate (PET) tubes, and in Example 3, BNP is measured in plastic tubes. In all of these Examples, BNP is measured in containers in the absence of any degradation-inhibiting agents.
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In the Office Action dated February 5, 2003, the Examiner writes, "It is the examiners position that none of the above citations provide any written description directed to excluding anything added to the assay." The Examiner's rejection is legally insufficient. It is a well-established tenant of U.S. patent practice that *ipsis verbis* disclosure is not necessary to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. Instead, the disclosure need only reasonably convey to persons skilled in the art that the inventor had possession of the subject matter in question. In re Edwards, 568 F.2d 1349 (CCPA 1978). Furthermore, if the specification contains a description of the claimed invention, albeit not in *ipsis verbis* (in the identical words), then the examiner or Board, in order to meet the burden of

proof, must provide reasons why one of ordinary skill in the art would not consider the description sufficient. In re Wertheim, 541 F.2d 257 (CCPA 1976). In the instant case, the Examiner fails to provide a reasonable basis challenging the adequacy of the written description, given the disclosure as a whole. The Examiner merely states, "...none of the above citations provide any written description..." For this reason, the Examiner has failed to meet his burden under 35 U.S.C. § 112, second paragraph.

The Examiner appears to base his assertion on his argument that "a negative limitation requires the highest degree of written description." However, the Examiner cites no authority for his argument, either in U.S. case law or in the Manual of Patent Examining Procedure (MPEP). Applicants therefore respectfully submit that the Examiner has no legal authority to make the above statement and haphazardly apply it to the instant case.

Alternatively, claim 5 should at least be considered allowable since "aprotinin" is literally recited on page 4, lines 18-19 of the specification, as noted above.

For the above reasons, Applicants respectfully submit that the claims fully comply with 35 U.S.C. § 112, first paragraph. Withdrawal of the instant rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

The Examiner maintains the rejection of claims 1-6 under 35 U.S.C. §103(a), for allegedly being obvious over the combination of Lindberg et al. (*Pharmacology & Toxicology*) in view of Clerico et al. (*Clinical Chemistry*). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Clerico et al. discloses that a protease inhibitor, such as aprotinin, can suppress the degradation of natriuretic peptides by a substance such as a protease. Lindberg et al. discloses that natriuretic peptides adsorb to the surface of a container coated with silicone. Neither Clerico et al. nor Lindberg et al. disclose or suggest that a use of a container coated with silicone or plastic can suppress the degradation of natriuretic peptides by a substance such as a protease. The present invention is based on the new finding that the degradation of natriuretic peptides by a substance such as a protease can be suppressed during measurement **without the need for degradation-inhibiting agents** by placing the natriuretic peptides in a container coated with silicone or plastic.

In fact, as pointed out in previously filed Replies, both Lindberg et al. and Clerico et al. necessarily require the use of degradation-inhibiting agents such as aprotinin or HSA, whereas the present invention excludes the use of such degradation inhibiting agents. In addition, Lindberg et al. expressly teaches away from excluding a degradation-inhibiting agent. For example, on page 281, last paragraph, Lindberg et al. discloses, "Thus, adsorption of ANP to materials used in the experimental situation is a factor of importance, entailing an obvious risk of distorting experimental results. This source of error can easily be avoided by the addition of HSA, as has been shown in this work."

In the Office Action dated February 5, 2003, the Examiner makes two assertions. First, the Examiner argues, "No invention is seen in not adding the known inhibitors." Apparently, it is the Examiner's position that since adding the inhibitors in his view is known in the art, then conversely, not adding the inhibitors in his view would be obvious.

Applicants strongly disagree with the Examiner on this point, and submit that he is not making a proper rejection under 35 U.S.C. § 103. Under 35 U.S.C. § 103, the prior art must disclose or suggest each element of the claims. Here, there is no suggestion or disclosure in the prior art to not add the inhibiting agents. Thus,

the Examiner lacks at least this element of a proper obviousness rejection.

Furthermore, the Examiner cannot merely state that "the lack of addition of the inhibitors would have the expected result" based upon his own opinion without any rationale and/or reference in support thereof. It appears as though the Examiner is attempting to rely on what he considers to be "common sense" in stating that excluding inhibitors from the container is obvious. However, the Examiner's reliance on "common sense" is clearly improper. "It is **never** appropriate to rely solely on 'common knowledge' in the art without evidentiary support in the record, as the principal evidence upon which a rejection is based [emphasis added]."¹ U.S. Pat. & Trademark Off., Manual Pat. Examining Proc. § 2144.03 (8th ed. rev. 1 2003). As held in by the Court of Appeals for the Federal Circuit, "[T]he Board cannot simply reach conclusions based on its own understanding or experience--or on its assessment of what would be basic knowledge or common sense." In re Zurko, 258 F.3d 1379, 1385 (Fed. Cir. 2001). See also In re Sang Su Lee, 277 F.3d 1338 (Fed. Cir. 2002), wherein the court stated that the Board's reliance on "common sense" in maintaining an obviousness rejection failed to comport with the USPTO's duty under the Administrative Procedure Act.

In the instant case, the Examiner has simply failed to produce any evidence that it would obvious to exclude the addition of degradation-inhibiting agents when the references relied upon all necessarily require the use of degradation-inhibiting agents. "Deficiencies of the cited references cannot be remedied by the Board's general conclusions about what is 'basic knowledge' or "common sense." In re Zurko, at 1385.

Second, the Examiner argues that the claims are written with open-ended "comprising" terminology. However, the Examiner ignores that the claims, whether or not they recite "comprising," specifically exclude degradation-inhibiting agents. It is not possible to not exclude the degradation-inhibiting agents on one hand by reciting comprising but exclude degradation-inhibiting agents on the other hand by a specific recitation thereof. Applicants respectfully submit that the Examiner that his logic is flawed. Alternatively, newly added claims 9-11 should at least be considered allowable since they recite the closed-language transitional phrase "consisting of."

For these reasons, Applicants respectfully submit that the present invention is not obvious over the cited prior art references. Withdrawal of the instant rejection is therefore respectfully requested.

Summary

All of the present claims define patentable subject matter such that this application should be placed into condition for allowance. Early and favorable action on the merits of the present application is thereby requested.

If there are any minor matters precluding allowance of the present application which may be resolved by a telephone discussion, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at (703) 205-8000.

Attached hereto is a marked-up version of the changes made to the application by this Reply.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of one (1) month to June 5, 2003, in which to file a reply to the Office Action. The required fee of \$110.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees

Appl. No. 09/530,013

required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17;
particularly, extension of time fees.

Respectfully submitted,

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Attachment: Version with Markings to Show Changes Made

CLAIM VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

The claims have been amended as follows:

1. (Five Times Amended) A method for inhibiting the degradation of mammalian natriuretic peptides in a specimen, comprising:

placing the specimen into a container in the absence [excluding the addition] of any degradation-inhibiting agents, wherein the face coming into contact with the specimen is made of or coated with a material selected from the group consisting of silicone and plastics,

wherein said material inhibits the activation of a substance, which [substance if not] once activated, degrades [cannot degrade] the mammalian natriuretic peptides [and is selected from the group consisting of silicone and plastics].

5. (Three Times Amended) A method for inhibiting the degradation of mammalian natriuretic peptides in a specimen, comprising:

placing the specimen into a container in the absence of aprotinin [excluding the addition of any degradation-inhibiting

agents], wherein the face coming into contact with the specimen is made of or coated with a material selected from the group consisting of silicone and plastics,

wherein said material inhibits the activation of a substance, which [substance if not] once activated, degrades [cannot degrade] the mammalian natriuretic peptides [and is selected from the group consisting of silicone and plastics, and

wherein said specimen does not contain aprotinin].

6. (Four Times Amended) A method for measuring mammalian natriuretic peptides in a specimen, comprising the steps of:

placing the specimen into [employing] a container in the absence [excluding the addition] of any degradation-inhibiting agents, wherein the face coming into contact with the specimen is made of or coated with a material selected from the group consisting of silicone and plastics [upon handling the specimen, comprising a material], wherein said material inhibits the activation of a substance, which [substance if not] once activated, degrades [cannot degrade] the mammalian natriuretic peptides [and is selected from the group consisting of silicone and plastics]; and

Appl. No. 09/530,013

measuring the mammalian natriuretic peptides by standard means.

Claims 9-11 have been added.